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Ethnicity and assisted reproductive technologies

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SUMMARY

Racial and ethnic disparities have been reported in every field of medicine. High costs associated with infertility treatment and restricted access to care has made assisted reproductive technologies particularly susceptible and vulnerable to disparity. Despite advances in the field, emerging literature has continued to demonstrate poorer outcomes in minority women receiving treatment with assisted reproductive technologies.

Healthcare disparities are a pervasive problem in the USA. The Institute of Medicine has documented the existence of health disparities in many areas, including reproductive health [1]. This discussion will focus on infertility, a common health problem that affects approximately 1 million American women from all racial, ethnic and socioeconomic backgrounds, and *in vitro* fertilization (IVF) [2]. The high cost of treatment, particularly with IVF, the limited access to services and variation in utilization by different ethnic groups make this area especially prone to disparities. Although generally, research in the area of infertility and, specifically, assisted reproductive technologies (ART) is expanding, only a limited number of studies have focused on racial differences in patients seeking infertility evaluation and treatment in the USA. Many of these investigations have been limited to black and white women, as these are the two largest racial groups receiving infertility treatments in the USA. The majority of these studies found lower utilization of ART, as well as ethnic differences in infertility diagnosis [3–7]. The aim of this review is to examine disparities specifically in the area of ART, particularly as they relate to disparities in both access and outcomes.

This discussion will begin with a review of the scope of the problem, followed by an examination of access and utilization of ART and will end with a summary of ethnic differences and outcomes.

The National Survey of Family Growth found that 7.4% of married women in the USA suffered from infertility [2]. The highest prevalence of infertility was found among African-American women at 11.5% [2]. Despite a higher risk of infertility, this group of women was less likely to receive treatment for infertility [2]. The following sections will examine issues related to access and utilization.

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Access/utilization of ART services

Costs of IVF are high. The average cost of IVF in the USA is approximately US\$12,513 per cycle, while the cost per live birth is estimated at \$41,132 [8]. These costs are prohibitive and make infertility treatments impractical, if not impossible, for many couples, especially low-income families [9,10]. In Australia and Scandinavia, countries where out-of-pocket expenses are kept low, levels of utilization met the expected demand; in North America, only 24% of the estimated demand was met [8].

The reasons minority women are less likely to access ART include cost, education and cultural beliefs. Several recent studies have shown that African-American women wait much longer before seeking treatment for fertility services [6]. As a result of a higher incidence of tubal factor, African-American and Hispanic women are also more likely to require ART, specifically IVF, in order to conceive. In addition, African-American and Hispanic women are more likely to have lower levels of education and household income levels when compared with white women seeking infertility services [6]. When examining barriers to infertility care, inability to pay for infertility treatment was a concern expressed by minority women [11]. Hispanics and African-American women also found it hard to find a physician and arrange leave from work [11]. Hispanic women specifically have concerns regarding communication barriers/limitations, continuity of care, difficulty scheduling follow-up appointments and limited accessibility to treatment [12].

In lower-cost, enhanced-access-to-care environments, some minority groups increase their utilization of ART. Studies conducted at military facilities, where access to care is increased due to more affordable infertility services for Department of Defense beneficiaries, allow an examination of ART service utilization [5,13]. These studies found an increase in utilization of ART in African-American, but not Hispanic women.

Several recent studies have examined the impact of insurance coverage on access and utilization. The laws governing these insurance mandates for infertility services vary considerably depending on the state. Currently, only three states have universal mandates, which require that all insurance policies cover ART [14]. Several other states have restricted mandates that direct some policies to cover ART, while a few states have 'other' mandates that require insurance companies to pay for some infertility treatments, but not IVF [14]. Universal insurance mandates have resulted in large overall increases in IVF utilization in areas where IVF services are covered by insurance [14]. Most of the literature, however, did not examine utilization within minority communities.

In Massachusetts (USA), which serves as an example of the impact of insurance mandates, a survey demonstrated that the majority of women who sought infertility treatment were white, highly educated and wealthy [15]. This illustrates that, even when costs are lowered and access is increased, Caucasian women from higher socioeconomic status (SES) groups will disproportionately utilize these services.

In a study by Greil *et al*, the investigators attempted to better identify and understand factors related to seeking treatment for infertility [16]. This study utilized data obtained from the National Survey of Fertility Barriers, which is a telephone survey designed to examine behavioral, emotional and social factors involving reproductive choices and infertility among American women. Black and Hispanic women had lower incomes, less education and were less likely to have health insurance. Attitudes toward infertility, specifically the stigma associated with the diagnosis, were assessed by infertility stigma scores. These scores were determined by combining responses to statements such as, "people who can't get pregnant without medical help often feel inadequate" [16]. Both African-American and Hispanic women had higher infertility stigma scores. All minority groups had more ethical

concerns regarding infertility than whites. African-Americans were less likely to have primary infertility, more likely to have never been married, less likely to have infertility with intent and typically had less encouragement from their partners/family to seek out treatment. Conversely, Asian women were very similar to white women except that they were more educated and had more ethical concerns related to infertility [16]. These social and individual cues may help explain why minority women underutilize infertility services.

Arab-American and African-American populations were found to have common obstacles. Both groups have an increased risk of infertility related to environmental factors, including residing in urban areas where exposure to reproductive toxins is higher. In addition, behavioral factors, including smoking, drug use and obesity may play a role. Both cultures value having children and parenthood is desirable; consequently, infertility strongly affects both men and women and their status in their communities. Both groups have been exposed to discriminatory practices and may have trust issues with the healthcare system [10]. Distrust is an issue in other minority groups as demonstrated in a study of Hispanic patients, which indicated a high level of distrust of physicians [17].

The medical establishment and the non-medical community also play a role in issues of access and utilization. In America, some minorities are viewed as hyperfertile and infertility may be viewed as a condition that affects only wealthy white couples [10,18]. In addition, some infertility clinics may not offer treatment to same-sex couples, single women or individuals with nontraditional lifestyles [10]. Studies have suggested that physicians' attitudes are affected by the race and SES of patients [19]. African-American patients are more likely to be perceived as less intelligent/educated than Caucasians, even after controlling for SES. Patients with lower SES were perceived as more irrational and less likely to be compliant than their wealthier counterparts. Such perceptions of patients can affect the care received [19]. This study illustrates the need for cultural competency training for all healthcare providers.

ART outcomes

African-Americans

Multiple studies regarding ART outcome in African-Americans have been conducted. There have only been a few studies that have noted no differences in outcomes when comparing African-American and Caucasian women. A retrospective study comparing outcomes in 24 African-American patients and 273 white patients found that implantation rates in African-American women were significantly higher (71 vs 48%) [20]. This is the only study that has actually shown more successful outcomes after ART in African-Americans. Another retrospective cohort study revealed no statistical differences in the percentage of ectopic pregnancies, miscarriages or live birth rates among ethnic groups [21]. Of note, although this study examined over 1000 cycles in white women, the number of African-Americans (43), Hispanics (18) and Asians (35) was very small [21]. A university-based study examined African-American and Caucasian patients and found no differences in implantation, pregnancy and live birth rates between the two groups [22]. This study was conducted in Washington, DC (USA), which has a large percentage of affluent African-Americans; therefore, the authors speculated that their data are less likely to be influenced by socioeconomic factors that could confound these results [22].

The vast majority of the literature in this area has shown worse ART outcomes among African-American women compared with Caucasian women. In 2000, Sharara and McClamrock examined black and white women pursuing infertility treatment in an inner city at a university-based programme [7]. This was the first study of its kind in the USA. The two groups were similar in age and day 3 follicle-stimulating hormone level, but black

women were more likely to have a longer duration of infertility and a higher BMI. They also required more aggressive ovarian stimulation. While white women had a higher incidence of endometriosis and male-factor infertility, African-American women had a much higher incidence of tubal-factor infertility. Despite similar numbers of oocytes retrieved and embryos transferred, black women had lower implantation rates, as well as clinical and ongoing pregnancy rates (9.8, 19.2 and 14.9% in blacks vs 23.4, 42.2 and 38.8% in whites, respectively) [7].

Feinberg and colleagues conducted a retrospective cohort study examining outcomes in black and white women [5]. Again, black women were noted to have a higher rate of tubal-factor infertility. In this study, they also had a higher rate of leiomyomata. African-American women had a clinically significant decrease in live birth rate, but it did not reach statistical significance. They were also found to have an increase in spontaneous abortions. All women with fibroids, regardless of race, were noted to have a reduction in clinical pregnancy rate and implantation rate [5].

In a Society for Assisted Reproductive Technology (SART) database review of 80,390 cycles, 4.6% of the cycles involved African-American women, 85.4% involved Caucasian women and 11.9% involved women of other races [4]. The final analysis reviewed over 72,000 cycles. Regarding the etiology of infertility, African-Americans were more likely to have tubal disorders and uterine-factor infertility compared with their white counterparts who were more likely to have a diagnosis of endometriosis, polycystic ovarian syndrome and male-factor infertility. In women undergoing fresh nondonor embryo cycles, the overall live birth rate per cycle was only 18.7% in black women compared with 26.3% in white women [4]. Black women were again found to have higher rates of spontaneous miscarriage. Interestingly, in frozen embryo transfers, the live birth rates were not different. Csokmay *et al.* also found a significant difference in live birth rates (16.7% in African-Americans vs 39.7% in Caucasians) during fresh cycle transfers; however, in frozen blastocyst transfers, no differences were identified [23].

There have been several postulated explanations for the disparity in ART outcomes in African-American women. African-American women have been found to have a greater incidence of tubal-factor infertility, as well as an increased likelihood of leiomyomas [7,23]. However, after controlling for tubal- and uterinefactor infertility, blacks have actually been found to have an independent risk factor for inability to achieve a live birth [4,24].

Obesity has also been identified as a potential factor in the poorer outcomes seen in African-American women. Unfortunately, obesity rates in black women are high; Flegal *et al.* found that 49.6% of non-Hispanic black women were obese vs 33% in non-Hispanic white women [25]. Obesity has been shown to adversely affect menstrual regularity and is associated with decreased fecundity, increased spontaneous abortions and decreased clinical pregnancy rates in patients undergoing ART [26–29]. In one study, which included BMI information, black women had higher BMIs, longer duration of infertility and higher incidence of tubal-factor infertility [7]. Another study found that all obese women were less likely to have a clinical pregnancy, but rates of clinical pregnancy were further reduced in African-American, Asian and Hispanic women [30].

Hispanics

Few studies have been conducted comparing outcomes after ART in Hispanic women. Of those that have been reported, there is some controversy regarding whether or not differences in outcomes truly exist. A recent study reviewed data from 134 Hispanic women and 301 Caucasian women, but did not note any significant difference in clinical pregnancies or live birth rates [31]. The Hispanic patients were more likely to have an

infertility diagnosis of tubal-factor infertility, while non-Hispanic white women were more frequently diagnosed with endometriosis [31]. Bendikson *et al.* did not find any difference in outcomes among Hispanic women, but this study was based upon a small sample of only 18 Hispanic women [21].

Feinberg *et al.* documented lower utilization of infertility services in Hispanic versus Caucasian women, despite equal access to care [32]. There were no differences, however, in infertility diagnosis or ART cycle parameters, nor in clinical pregnancy, live birth, spontaneous abortion or implantation rates. Another multicenter study conducted at military treatment facilities again documented lower utilization among Hispanic patients, as well as a decrease in clinical pregnancy rates and live birth rates [13].

Asians

Analyzing ART-outcome data among Asian women is complicated by the heterogeneity of this group. Some studies group all Asian women together regardless of their ethnic background (Chinese, Japanese and Indian, among others), making analysis and interpretation of the data difficult. The alternative, to categorize patients by more specific racial and ethnic categories, results in numbers that are often too small to provide useful data.

In a retrospective study of Caucasian and Asian women undergoing intrauterine insemination, the Asian group had significantly lower pregnancy rates than did the Caucasian women [33]. The only significant difference in characteristics between the two groups was that >40% of the Asian women had suffered from infertility for longer than 2 years.

In a comparison of IVF success rates in Caucasian and Asian patients, demographic characteristics were found to be very similar. Asian women once again had a lower clinical pregnancy rate, as well as live birth rate. The authors concluded that Asian race was an independent risk factor of poorer outcome after ART; however, no clear reason for these differences could be documented (Table 1) [34].

Another study evaluated 180 blastocyst transfer cycles among Asian and Caucasian women [35]. The Asian group consisted of women of Japanese, Chinese and Filipino backgrounds. The women in both groups of the study were very similar in their response to therapy and embryo quality. However, Asian women had significantly lower rates of implantation, clinical pregnancy and live births. Gleicher *et al.* examined Chinese and Caucasian oocyte donors [36]. These groups were similar in age, but the Chinese donors had a higher likelihood of premature ovarian aging, which could possibly explain why this group had poorer outcomes after ART.

In a study of live birth rates of Indian and Caucasian women, Indian women were found to have significantly lower live birth rates despite the use of high-quality embryos [37]. In a study of Indian and Caucasian women with polycystic ovarian syndrome, the south-Asian women were noted to have a greater sensitivity to gonadotropins and produced a higher number of mature oocytes, but had significantly lower fertilization and ongoing clinical pregnancy rates [38]. Unlike patients from western countries, a higher incidence of genital tuberculosis has been found in the Indian population. This diagnosis, which is rare in most of the world, has an extremely poor prognosis [39,40]. Women with pelvic tuberculosis frequently present to care secondary to tubal-factor infertility [40,41]. The prevalence has been reported anywhere from 1 to 19% [40]. This condition is becoming more frequent in western countries due to the increase in individuals migrating from developing countries and the increase in drug-resistant tuberculosis [40,41]. A high index of suspicion for genital

tuberculosis may be warranted in young Indian women with unexplained tubal-factor infertility and may be a factor in poor obstetrical outcomes in this group.

Conclusion

The largest study to date used data from the SART Clinic Outcome Reporting System and examined outcomes of 139,027 nondonor ART cycles in African–American, Asian, Hispanic and Caucasian women. Outcomes of the minority groups were compared with those of Caucasian women [42]. The major findings in this study were:

- Lower clinical pregnancy rate in Asian women;
- Lower live birth rates in African–American, Hispanic and Asian women;
- Higher likelihood of preterm deliveries in African–American and Hispanic women;
- Higher rates of intrauterine growth restriction in African–American, Hispanic and Asian women [42];

The existing data suggest that there are ethnic/racial differences in infertility incidence, diagnosis and outcomes with treatment [4,5,7,13,33–35,37,42]. One of the major challenges of examining these disparities is a lack of a universally acceptable nomenclature for categorization of patients. Another obstacle to collecting this data is the low compliance rate of reporting race and ethnicity. The SART database does not require race/ethnicity; as a result, this information is missing for a large percentage of patients. One recent publication based on the SART database estimated that race and ethnicity information is missing in approximately one-third of reported cycles [30]. The American Society for Reproductive Medicine Health Disparities Special Interest Group recently examined several articles that utilized SART Clinic Outcome Reporting System data in an effort to report information regarding disparities in access and outcomes of infertility treatments. Data regarding race or ethnicity was missing from more than 35% of cycles, largely due to practitioners not recording this information [43]. The authors are now encouraging universal reporting of race/ethnicity in the SART database.

Under-represented minorities in the USA have been demonstrated to have differences in access to healthcare and health-related outcomes. Further studies, specifically related to infertility, must be conducted in an attempt to document the extent and nature of the disparities and to address them. The solution to the problem begins with the development of a useable system of race and ethnicity identification and accurate reporting of race and ethnicity in all studies. As per the NIH guidelines, studies in this area should be conducted that include a representative sample of under-represented minorities and efforts should be made to actively recruit minority women for participation in these studies [44].

Obesity has been noted to negatively affect fertility in multiple studies [26–29]. Recently, it has also been linked to further impairments in reproductive outcomes in minority women [30]. As the obesity epidemic worsens, more and more women will be plagued by obesity and its sequelae; therefore, obesity will continue to adversely affect the health status of women not only in this country, but across the world. Public health initiatives, designed in a culturally competent fashion, could improve BMI parameters and positively impact patients' health in general, as well as improving their chances of conception.

Well-designed studies regarding race and reproductive outcomes will hopefully identify links that explain the causes of disparate reproductive outcomes, further expanding our knowledge and identifying effective strategies.

Future perspective

Minority women suffering from infertility are often hesitant to pursue infertility treatment for a variety of reasons. Physicians and practitioners involved in reproductive healthcare must continue to work to eliminate access-to-care barriers. Community outreach and education of primary care providers, particularly related to specialty care referral, could greatly enhance the likelihood that disadvantaged patients may actually seek care.

Multiple studies have observed poorer reproductive outcomes in African–American, Hispanic and Asian women when compared with Caucasians. However, these studies have not identified a specific cause that could account for these outcomes. Further studies must be conducted in order to determine which factors contribute to these disparities. Identifying the causative factors will be instrumental in identifying effective solutions. Equal access, improved reproductive outcomes and the elimination of healthcare disparities should be our goal.

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■ ■ of considerable interest

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Practice points

- Access to care continues to be an issue in minority women with infertility.
- Enhanced access to care does not necessarily translate into increased utilization of infertility services in all minority groups.
- Cultural issues may influence access to care, particularly among Hispanic patients.
- Higher BMIs, increased frequency of fibroids and higher likelihood of tubal factor infertility may play a role in poorer outcomes among African-American women.
- Asian women are a heterogeneous group, which makes it a difficult population to study.
- Pelvic tuberculosis may be linked to poor outcomes in women from south Asia.
- Medical schools and residency programmes must continue to stress cultural competency.
- Further study is needed to address healthcare disparities among infertile women.

Table 1

Comparison of assisted reproductive technology outcomes among African–Americans, Hispanics and Asians.

Study (year)	n/total n	LBR vs LBR (%) [†]	Ref.
African–Americans			
Fujimoto <i>et al.</i> (2010)	8903/139,027	32.0 vs 40.1	[42]
Seifer <i>et al.</i> (2008)	1839/33,888	20.7 vs 28.4	[4]
Hispanics			
Fujimoto <i>et al.</i> (2010)	8969/139,027	37.3 vs 40.1	[42]
McCarthy-Keith <i>et al.</i> (2010)	81/1929	33.3 vs 45.7	[13]
Asians			
Fujimoto <i>et al.</i> (2010)	13,671/139,027	30.9 vs 40.1	[42]
Purcell <i>et al.</i> (2007)	1429/27,272	26.9 vs 34.9	[34]

[†] Compared with Caucasian women.

LBR: Live birth rate.